SEQ ID NO:4.--

C1

--3. (Amended) An antisense oligonucleotide or analog thereof comprising nucleotide sequence SEQ ID NO:4.--

--4. (Amended) The antisense oligonucleotide of claim 3, wherein the nucleotide sequence comprises nucleotide sequence SEQ ID NO:19.--

A mark-up copy of the amendments to the claims is attached hereto as **Exhibit A**.

Remarks

Claims 1-47 are currently pending in the above-identified application. Applicants have, hereinabove, amended claims 1-4 merely to refer to nucleotide sequences by sequence identifiers, as requested by the Examiner in the February 24, 2003 Office Action issued in connection with the above-identified application. As such, applicants maintain that the amendments to the claims raise no issue of new matter and respectfully request that this Amendment be entered.

Restriction Requirement Under 35 U.S.C. §121

In the February 24, 2003 Office Action, the Examiner stated that restriction to one of the following inventions is required under 35 U.S.C. §121:

I. Claims 1-16, and 42-47, drawn to antisense oligonucleotides or analogs thereof and pharmaceutical compositions thereof,

classified in class 536, subclass 24.5.

II. Claims 17-41, drawn to methods comprising the introduction of an antisense oligomer into a cell for treatment purposes, classified in class 514, subclass 44.

The Examiner stated that the inventions are distinct, each from the other because of the following reasons:

The Examiner stated that inventions I and II are related as product and process of use. The Examiner stated that the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP §806.05 (h)). The Examiner stated that in this case the antisense oligonucleotide and compositions thereof according to invention I can be used in a method other than that set forth in invention II, for example, as a probe in method to assay for the expression of bcl-xl nucleic acid in a cellular sample.

Applicants note that the claimed sequences block or inhibit bcl-xl expression.

The Examiner stated that because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. The Examiner stated that in addition to the restriction requirement set forth above, pursuant to 35 U.S.C. §121 and 37 C.F.R. §1.141, the antisense

oligonucleotide sequences listed in claims 1-4 are subject to restriction. The Examiner stated that claims 1-47 read on the antisense oligonucleotide sequence as set forth in Figures 1, 2A and 2B of the specification as filed. The Examiner also stated that although the antisense sequences claimed are disclosed as each targeting and inhibiting the expression of the same gene (bcl-xl), the instant antisense sequences are considered to be unrelated, since each antisense sequence claimed is structurally and functionally independent and distinct for the following reasons: each antisense sequence has a unique nucleotide sequence, each antisense sequence targets a different and specific region of the bcl-xl gene, and each antisense, upon binding to bcl-xl mRNA, functionally regulates the expression of the bcl-xl gene to varying degrees (per applicant's Table 1 in the specification as filed, page 37).

The Examiner stated that, therefore, a search of more than one (1) of the antisense sequences recited in claims 1-4 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed antisense sequences. The Examiner stated that in view of the foregoing, one (1) antisense sequence is considered to be a reasonable number of sequences for examination. The Examiner stated that, accordingly, applicants are required to elect one (1) antisense oligonucleotide sequence recited in one of claims 1-4 to be searched with the elected invention. The Examiner stated that this is not an election of species but a restriction requirement; therefore applicants must amend the remaining pending claims to recited the particular elected antisense oligonucleotide and to remove all reference to non-elected inventions.

The Examiner also stated that applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined, either invention I or II, and a further election of antisense oligonucleotides to be searched with the elected invention, even though the requirement be traversed (37 C.F.R. §1.143).

In response to this restriction requirement, applicants hereby elect, with traverse, to prosecute the invention of Examiner's Group I, drawn to antisense oligonucleotides or analogs thereof and pharmaceutical compositions thereof.

Applicants note that 35 U.S.C. §121 states, in part, that "[i]f two or more independent and distinct inventions are claimed in one application, the Commissioner may require application to be restricted to one of the inventions." [Emphasis added]. Applicants request that the restriction requirement with respect to the sequences be withdrawn in view of the fact that the sequences are not independent.

Under M.P.E.P. §802.1, "independent" means "there is no disclosed relationship between the subjects disclosed, that is, they are unconnected in design, operation, and effect...". The sequences of are related in that they are drawn to similar compounds within the same group. The sequences will be classified in the same class and subclass. In addition, they are functionally identical, in that they all perform the same function of inhibiting expression of bcl-xl. The extent to which they inhibit bcl-xl is not relevant to a search of relevant art.

Applicants therefore respectfully assert that two or more

independent and distinct inventions have not been claimed in the subject application because the groups are not independent under M.P.E.P. §802.01. Therefore, restriction is improper under 35 U.S.C. §121.

Additionally, applicants point out that under M.P.E.P. §803, the Examiner must examine the application on the merits, even though it includes claims to distinct inventions, if the search and examination of an application can be made without serious burden. There are two criteria for a proper requirement for restriction, namely (1) the invention must be independent and distinct; AND (2) there must be a serious burden on the Examiner if restriction is not required.

Applicants maintain that there would not be a serious burden on the Examiner if restriction were not required. Furthermore, identifying antisense sequences showing complementarity to a single disclosed sequence will necessarily identify art for all of such sequences and compositions. Applicants respectfully contend that there is no serious burden on the Examiner to examine sequences in the subject application, and respectfully request that the Examiner examine the entire application on the merits. Applicants further maintain that such a search is not a complex search, as alleged by the Examiner.

Applicants maintain that claims 1-16 and 42-47 claiming disclosed sequences define a single inventive concept. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the sequence restriction requirement and examine claims 1-16 and 42-47 on the merits.

The Examiner stated that claims 1-4 are objected to for failing to

recite the appropriate sequence identifiers. The recitation of Figures 1, and 2A-2B in claims 1-4 to indicate the antisense oligonucleotide sequences set forth in these figures is inappropriate since incorporation by reference to a specific figure or table is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. The Examiner stated that incorporation by reference is a necessity doctrine, not for applicant's convenience, (See MPEP § 2173.05(s)), and that in the instant case the most practical way to define a nucleotide sequence is by reference to its SEQ ID NO: as per 37 C.F.R. §§1.821 through 1.825.

In response, applicants have hereinabove amended claims 1-4 to refer to SEQ ID NO.s. In addition, in response to the sequence restriction requirement imposed in the February 24, 2003 Office action, applicants have amended the claims to refer to a single sequence. In light of this, applicants note that SEQ ID NO:4 identified in claims 1-3 has the same nucleotide sequence described in SEQ ID NO:19 identified in claim 4. The different sequence identifiers provide different information regarding the internucleoside linkages and derivatization of the sequence.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Communication. If any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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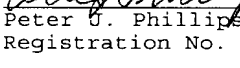

3/24/03
Peter J. Phillips Date
Registration No. 29,691

Mark-Up Copy of the Amendments to the Claims

Claims 1-4 have been amended as follows:

--1. (Amended) An antisense oligonucleotide or analog thereof comprising 10 or more contiguous bases or base analogs from the sequence of bases of [sequence A, B, C, D, E, F, G, H, I, J, K, L, or M of Figure 1] SEQ ID NO:4.--

--2. (Amended) An antisense oligonucleotide or analog thereof comprising a sequence having 90% of greater identity to [sequence A, B, C, D, E, F, G, H, I, J, K, L, or M of Figure 1] SEQ ID NO:4.--

--3. (Amended) An antisense oligonucleotide or analog thereof comprising nucleotide sequence [sequence A, B, C, D, E, F, G, H, I, J, K, L, or M of Figure 1] SEQ ID NO:4.--

--4. (Amended) The antisense oligonucleotide of claim 3, wherein the nucleotide sequence comprises nucleotide sequence [A, A', B, C, C', D, E, E', F, G, G', H, H', I, I', J, K, K', L, L', M, or M' of Figures 2A and 2B] SEQ ID NO:19.--